

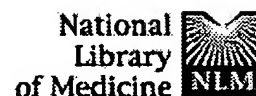
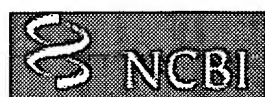
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<input type="checkbox"/>	L36	5789230.pn. and papilloma virus	1
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	<i>DB=PGPB; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L32	deleted "L1" epitope	0
<input type="checkbox"/>	L31	deleted "L1" antigen	0
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<input type="checkbox"/>	L26	empty virus like particles and papillomavirus	0
<input type="checkbox"/>	L25	L2 and papillomavirus	0
	<i>DB=EPAB; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L24	WO-9746693-A1.did.	1
<input type="checkbox"/>	L23	WO-9746693-A1.did.	1
	<i>DB=USOC; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L22	major capsid protein and human papilloma virus modified and nonimmunogenic	0
	<i>DB=EPAB; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L21	major capsid protein and human papilloma virus modified and nonimmunogenic	0
	<i>DB=JPAB; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L20	major capsid protein and human papilloma virus modified and nonimmunogenic	0
	<i>DB=DWPI; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L19	major capsid protein and human papilloma virus modified and nonimmunogenic	1
<input type="checkbox"/>	L18	major capsid protein of human papilloma virus modified to be nonimmunogenic	0
	<i>DB=EPAB; PLUR=YES; OP=ADJ</i>		
<input type="checkbox"/>	L17	ZA-200200886-A.did.	0

<input type="checkbox"/>	L16	EP-1222200-A1.did.	0
		<i>DB=DWPI; PLUR=YES; OP=ADJ</i>	
<input type="checkbox"/>	L15	Antonsson p.in.	4
		<i>DB=EPAB; PLUR=YES; OP=ADJ</i>	
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		<i>DB=DWPI; PLUR=YES; OP=ADJ</i>	
<input type="checkbox"/>	L12	Bloch M A.in.	2
<input type="checkbox"/>	L11	Bloch.in. virus like	0
<input type="checkbox"/>	L10	Bloch.in. gene therapy	0
<input type="checkbox"/>	L9	Bloch.in. VLP	0
<input type="checkbox"/>	L8	Bloch.in.	496
<input type="checkbox"/>	L7	Bloch.in. and papillomavirus	0
		<i>DB=USPT; PLUR=YES; OP=ADJ</i>	
<input type="checkbox"/>	L6	Bloch.in. and papillomavirus	1
<input type="checkbox"/>	L5	Bloch.in. and papilomavirus	0
<input type="checkbox"/>	L4	L2 and papillomavirus	1
<input type="checkbox"/>	L3	L2 and papillomairus	0
<input type="checkbox"/>	L2	empty virus like particles	8
<input type="checkbox"/>	L1	papillomavirus and virus like particles	137

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☐ 1: [Carter JJ, Wipf GC, Benki SF, Christensen ND, Galloway DA.](#) Related Articles, Links

Identification of a human papillomavirus type 16-specific epitope on the C-terminal arm of the major capsid protein L1.
 J Virol. 2003 Nov;77(21):11625-32.
 PMID: 14557648 [PubMed - indexed for MEDLINE]

☐ 2: [Christensen ND, Cladel NM, Reed CA, Budgeon LR, Embers ME, Skulsky DM, McClements WL, Ludmerer SW, Jansen KU.](#) Related Articles, Links

Hybrid papillomavirus L1 molecules assemble into virus-like particles that reconstitute conformational epitopes and induce neutralizing antibodies to distinct HPV types.
 Virology. 2001 Dec 20;291(2):324-34.
 PMID: 11878901 [PubMed - indexed for MEDLINE]

☐ 3: [White WI, Wilson SD, Palmer-Hill FJ, Woods RM, Ghim SJ, Hewitt LA, Goldman DM, Burke SJ, Jenson AB, Koenig S, Suzich JA.](#) Related Articles, Links

Characterization of a major neutralizing epitope on human papillomavirus type 16 L1.
 J Virol. 1999 Jun;73(6):4882-9.
 PMID: 10233949 [PubMed - indexed for MEDLINE]

☐ 4: [Combata AL, Touze A, Bousarghin L, Christensen ND, Coursaget P.](#) Related Articles, Links









Identification of two cross-neutralizing linear epitopes within the L1 major capsid protein of human papillomaviruses.
 J Virol. 2002 Jul;76(13):6480-6.
 PMID: 12050360 [PubMed - indexed for MEDLINE]

☐ 5: [Varsani A, Williamson AL, de Villiers D, Becker I, Christensen ND, Rybicki EP.](#) Related Articles, Links

Chimeric human papillomavirus type 16 (HPV-16) L1 particles presenting the common neutralizing epitope for the L2 minor capsid protein of HPV-6 and HPV-16.
 J Virol. 2003 Aug;77(15):8386-93.
 PMID: 12857908 [PubMed - indexed for MEDLINE]

☐ 6: [Christensen ND, Dillner J, Eklund C, Carter JJ, Wipf GC, Reed CA, Cladel NM, Galloway DA.](#) Related Articles, Links

Surface conformational and linear epitopes on HPV-16 and HPV-18 L1 virus-like particles as defined by monoclonal antibodies.
 Virology. 1996 Sep 1;223(1):174-84.
 PMID: 8806551 [PubMed - indexed for MEDLINE]

- ☐ 7: [Wang XM, Cook JC, Lee JC, Jansen KU, Christensen ND, Ludmerer SW, McClements WL.](#) [Related Articles, Links](#)
-  Human papillomavirus type 6 virus-like particles present overlapping yet distinct conformational epitopes.
J Gen Virol. 2003 Jun;84(Pt 6):1493-7.
PMID: 12771418 [PubMed - indexed for MEDLINE]
- ☐ 8: [McClements WL, Wang XM, Ling JC, Skulsky DM, Christensen ND, Jansen KU, Ludmerer SW.](#) [Related Articles, Links](#)
-  A novel human papillomavirus type 6 neutralizing domain comprising two discrete regions of the major capsid protein L1.
Virology. 2001 Oct 25;289(2):262-8.
PMID: 11689049 [PubMed - indexed for MEDLINE]
- ☐ 9: [Sadeyen JR, Tourne S, Shkreli M, Sizaret PY, Coursaget P.](#) [Related Articles, Links](#)
-  Insertion of a foreign sequence on capsid surface loops of human papillomavirus type 16 virus-like particles reduces their capacity to induce neutralizing antibodies and delineates a conformational neutralizing epitope.
Virology. 2003 Apr 25;309(1):32-40.
PMID: 12726724 [PubMed - indexed for MEDLINE]
- ☐ 10: [Christensen ND, Reed CA, Cladel NM, Hall K, Leiserowitz GS.](#) [Related Articles, Links](#)
-  Monoclonal antibodies to HPV-6 L1 virus-like particles identify conformational and linear neutralizing epitopes on HPV-11 in addition to type-specific epitopes on HPV-6.
Virology. 1996 Oct 15;224(2):477-86.
PMID: 8874508 [PubMed - indexed for MEDLINE]
- ☐ 11: [Volpers C, Sapp M, Snijders PJ, Walboomers JM, Streeck RE.](#) [Related Articles, Links](#)
-  Conformational and linear epitopes on virus-like particles of human papillomavirus type 33 identified by monoclonal antibodies to the minor capsid protein L2.
J Gen Virol. 1995 Nov;76 (Pt 11):2661-7.
PMID: 7595373 [PubMed - indexed for MEDLINE]
- ☐ 12: [Wang X, Wang Z, Christensen ND, Dillner J.](#) [Related Articles, Links](#)
-  Mapping of human serum-reactive epitopes in virus-like particles of human papillomavirus types 16 and 11.
Virology. 2003 Jun 20;311(1):213-21.
PMID: 12832218 [PubMed - indexed for MEDLINE]
- ☐ 13: [Kawana K, Matsumoto K, Yoshikawa H, Taketani Y, Kawana T, Yoshiike K, Kanda T.](#) [Related Articles, Links](#)
-  A surface immunodeterminant of human papillomavirus type 16 minor capsid protein L2.
Virology. 1998 Jun 5;245(2):353-9.
PMID: 9636375 [PubMed - indexed for MEDLINE]
- ☐ 14: [Touze A, El Mehdaoui S, Sizaret PY, Mouglin C, Munoz N, Coursaget P.](#) [Related Articles, Links](#)
-  The L1 major capsid protein of human papillomavirus type 16 variants affects yield of virus-like particles produced in an insect cell expression system.
J Clin Microbiol. 1998 Jul;36(7):2046-51.

PMID: 9650960 [PubMed - indexed for MEDLINE]

- ☐ 15: [Cason J, Patel D, Naylor J, Lunney D, Shepherd PS, Best JM, McCance DJ.](#) [Related Articles, Links](#)



Identification of immunogenic regions of the major coat protein of human papillomavirus type 16 that contain type-restricted epitopes.

J Gen Virol. 1989 Nov;70 (Pt 11):2973-87.

PMID: 2479716 [PubMed - indexed for MEDLINE]

- ☐ 16: [Chen Y, Ghim SJ, Jensen AB, Schlegel R.](#) [Related Articles, Links](#)



Mutant canine oral papillomavirus L1 capsid proteins which form virus-like particles but lack native conformational epitopes.

J Gen Virol. 1998 Sep;79 (Pt 9):2137-46.

PMID: 9747722 [PubMed - indexed for MEDLINE]

- ☐ 17: [Christensen ND, Kimbaurer R, Schiller JT, Ghim SJ, Schlegel R, Jensen AB, Kreider JW.](#) [Related Articles, Links](#)



Human papillomavirus types 6 and 11 have antigenically distinct strongly immunogenic conformationally dependent neutralizing epitopes.

Virology. 1994 Nov 15;205(1):329-35.

PMID: 7526536 [PubMed - indexed for MEDLINE]

- ☐ 18: [Kulski JK, Sadleir JW, Kelsall SR, Cicchini MS, Shellam G, Peng SW, Qi YM, Galloway DA, Zhou J, Frazer IH.](#) [Related Articles, Links](#)



Type specific and genotype cross reactive B epitopes of the L1 protein of HPV16 defined by a panel of monoclonal antibodies.

Virology. 1998 Apr 10;243(2):275-82.

PMID: 9568027 [PubMed - indexed for MEDLINE]

- ☐ 19: [Ludmerer SW, Benincasa D, Mark GE 3rd, Christensen ND.](#) [Related Articles, Links](#)



A neutralizing epitope of human papillomavirus type 11 is principally described by a continuous set of residues which overlap a distinct linear, surface-exposed epitope.

J Virol. 1997 May;71(5):3834-9.

PMID: 9094659 [PubMed - indexed for MEDLINE]

- ☐ 20: [Roden RB, Armstrong A, Haderer P, Christensen ND, Hubbert NL, Lowy DR, Schiller JT, Kimbaurer R.](#) [Related Articles, Links](#)



Characterization of a human papillomavirus type 16 variant-dependent neutralizing epitope.

J Virol. 1997 Aug;71(8):6247-52.

PMID: 9223527 [PubMed - indexed for MEDLINE]

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(FILE 'HOME' ENTERED AT 13:03:11 ON 12 AUG 2004)

FILE 'MEDLINE' ENTERED AT 13:03:19 ON 12 AUG 2004

L1	14951 S PAPILOMAVIRUS
L2	159 S VLP AND L1
L3	2173 S VIRUS LIKE PARTICLES
L4	321 S L3 AND L1
L5	53 S CARRIER AND L3
L6	46 S EMPTY AND L3
L7	26 S GENE THERAPY AND L3

L7 ANSWER 1 OF 26 MEDLINE on STN
 AN 2004135757 MEDLINE
 DN PubMed ID: 14973544
 TI DNA vaccine-encapsulated **virus-like particles**
 derived from an orally transmissible virus stimulate mucosal and systemic
 immune responses by oral administration.
 AU Takamura S; Niikura M; Li T-C; Takeda N; Kusagawa S; Takebe Y; Miyamura T;
 Yasutomi Y
 CS Department of Bioregulation, Mie University School of Medicine, Tsu, Mie,
 Japan.
 SO Gene therapy, (2004 Apr) 11 (7) 628-35.
 Journal code: 9421525. ISSN: 0969-7128.
 CY England: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200407
 ED Entered STN: 20040319
 Last Updated on STN: 20040722
 Entered Medline: 20040721
 AB Delivery of foreign genes to the digestive tract mucosa by oral
 administration of nonreplicating gene transfer vectors would be a very
 useful method for vaccination and **gene therapy**.
 However, there have been few reports on suitable vectors. In the present
 study, we found that plasmid DNA can be packaged in vitro into a
 virus-like particle (VLP) composed of open reading frame 2 of hepatitis E
 virus, which is an orally transmissible virus, and that these VLPs can
 deliver this foreign DNA to the intestinal mucosa in vivo. The delivery
 of plasmid DNA to the mucosa of the small intestine was confirmed by the
 results of immunohistochemical analyses using an expression plasmid
 encoding human immunodeficiency virus env (HIV env) gp120. After oral
 administration of VLPs loaded with HIV env cDNA, significant levels of
 specific IgG and IgA to HIV env in fecal extracts and sera were found.
 Moreover, mice used in this study exhibited cytotoxic T-lymphocyte
 responses specific to HIV env in the spleen, Payer's patches and
 mesenteric lymph nodes. These findings suggest that VLPs derived from
 orally transmissible viruses can be used as vectors for delivery of genes
 to mucosal tissue by oral administration for the purpose of DNA
 vaccination and **gene therapy**.
 CT Check Tags: Female; Support, Non-U.S. Gov't
 *AIDS Vaccines: GE, genetics
 Administration, Oral
 Animals
 Cell Line
 *Gene Therapy: MT, methods
 *Genetic Vectors: AD, administration & dosage
 *Hepatitis E virus: GE, genetics
 Immunity, Mucosal
 *Intestinal Mucosa: IM, immunology
 Mice
 Mice, Inbred BALB C
 *Open Reading Frames
 T-Lymphocytes, Cytotoxic: IM, immunology
 CN 0 (AIDS Vaccines); 0 (Genetic Vectors)

L7 ANSWER 2 OF 26 MEDLINE on STN
 AN 2003592752 MEDLINE
 DN PubMed ID: 14645925
 TI Murine pneumotropic virus VP1 **virus-like**
particles (VLPs) bind to several cell types independent of sialic
 acid residues and do not serologically cross react with murine

polyomavirus VP1 VLPs.

AU Tegerstedt K; Andreasson K; Vlastos A; Hedlund K O; Dalianis T; Ramqvist T
CS Department of Oncology-Pathology, Karolinska Institute, Cancer Center
Karolinska R8 : 01, Karolinska Hospital, SE-171 76 Stockholm, Sweden.
SO Journal of general virology, (2003 Dec) 84 (Pt 12) 3443-52.
Journal code: 0077340. ISSN: 0022-1317.

CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200401
ED Entered STN: 20031217
Last Updated on STN: 20040121
Entered Medline: 20040120

AB The ability of murine pneumotropic virus (MPtV) major capsid protein VP1 to form **virus-like particles** (VLPs) was examined. MPtV-VLPs obtained were used to estimate the potential of MPtV to attach to different cells and to assess some characteristics of the MPtV cell receptor. Furthermore, to evaluate if MPtV-VLPs could potentially complement murine polyomavirus (MPyV) VP1 VLPs (MPyV-VLPs) as vectors for prime-boost **gene therapy**, the capability of MPtV-VLPs to serologically cross react with MPyV-VLPs and to transduce DNA into cells was examined. MPtV VP1 obtained in a recombinant baculovirus system formed MPtV-VLPs readily. MPtV-VLPs were shown by FACS analysis to bind to different cells, independent of MHC class I antigen expression. In addition, MPtV-VLPs did not cause haemagglutination of red blood cells and MPtV-VLP binding to cells was neuraminidase resistant but mostly trypsin and papain sensitive, indicating that the MPtV receptor lacks sialic acid components. When tested by ELISA and in vivo neutralization assays, MPtV-VLPs did not serologically cross react with MPyV-VLPs, suggesting that MPtV-VLPs and MPyV-VLPs could potentially be interchanged as carriers of DNA in repeated **gene therapy**. Finally, MPtV-VLPs were shown to transduce foreign DNA in vitro and in vivo. In conclusion, the data suggest that MPtV-VLPs, and possibly also MPtV, bind to several different cell types, that binding is neuraminidase resistant and that MPtV-VLPs should potentially be able to complement MPyV-VLPs for prime-boost gene transfer in vivo.

CT Check Tags: Human; Support, Non-U.S. Gov't
Animals
*Antibodies, Viral: IM, immunology
Capsid Proteins: IM, immunology
*Capsid Proteins: ME, metabolism
Cell Line
Cercopithecus aethiops
Cross Reactions
DNA-Binding Proteins: ME, metabolism
Enzyme-Linked Immunosorbent Assay
Guinea Pigs
Hemagglutination
Histocompatibility Antigens Class I: ME, metabolism
Mice
N-Acetylneuraminic Acid
Neuraminidase: PD, pharmacology
Neutralization Tests
Papain: PD, pharmacology
Plasmids
Polyomavirus: IM, immunology
*Polyomavirus: ME, metabolism
Polyomavirus: UL, ultrastructure
Protein Binding
Receptors, Virus: CH, chemistry
Receptors, Virus: DE, drug effects

Receptors, Virus: ME, metabolism
 Trypsin: PD, pharmacology

RN 131-48-6 (N-Acetylneuraminic Acid)
 CN 0 (Antibodies, Viral); 0 (Capsid Proteins); 0 (DNA-Binding Proteins); 0
 (Histocompatibility Antigens Class I); 0 (Plasmids); 0 (Receptors, Virus);
 0 (polyomavirus capsid protein VP1); EC 3.2.1.18 (Neuraminidase); EC
 3.4.21.4 (Trypsin); EC 3.4.22.2 (Papain)

L7 ANSWER 3 OF 26 MEDLINE on STN
 AN 2003524218 MEDLINE
 DN PubMed ID: 14601522
 TI The use of **virus-like particles** for gene
 transfer.
 AU Petry Harald; Goldmann Claudia; Ast Oliver; Luke Wolfgang
 CS Berlex Biosciences, 2600 Hilltop Drive, PO Box 4099, Richmond, CA
 94804-0099, USA.
 SO Current opinion in molecular therapeutics, (2003 Oct) 5 (5) 524-8. Ref:
 53
 Journal code: 100891485. ISSN: 1464-8431.
 CY England: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 General Review; (REVIEW)
 (REVIEW, TUTORIAL)
 LA English
 FS Priority Journals
 EM 200403
 ED Entered STN: 20031107
 Last Updated on STN: 20040331
 Entered Medline: 20040330

AB A major challenge in the field of **gene therapy** is the
 development of new carrier/delivery systems that lack the disadvantages of
 current transfer systems. In the past, some time has been spent
 developing such modified or alternative vectors. A new candidate is
 represented by **virus-like particles** (VLPs).
 It has been shown that recombinant expression of the major structural
 proteins of many viruses leads to the formation of VLPs. Such VLPs
 exhibit morphology similar to the empty capsids of the virus from which
 they are derived. VLPs are non-infectious, have a similar tropism to the
 natural virus, and show comparable cellular uptake and intracellular
 trafficking. Since its discovery, VLP technology has gained importance in
 biomedical research. Although most investigations into VLP technology
 have dealt with vaccine development, some research groups have
 demonstrated that VLPs could also represent a useful **gene
 therapy** delivery system. This review will focus on studies
 performed with VLPs from members of the Papillomaviridae and
 Polyomaviridae families.

CT Check Tags: Human
 Animals
 DNA, Viral: ME, metabolism
 ***Gene Therapy**
 *Gene Transfer Techniques
 Genetic Vectors: GE, genetics
 Genetic Vectors: IM, immunology

AN 2003510481 MEDLINE
DN PubMed ID: 14557648
TI Identification of a human papillomavirus type 16-specific
epitope on the C-terminal arm of the major capsid protein
L1.
AU Carter Joseph J; Wipf Greg C; Benki Sarah F; Christensen Neil D; Galloway
Denise A
CS Program in Cancer Biology, Fred Hutchinson Cancer Research Center,
Seattle, Washington 98109-1024, USA.. jcarter@fhcrc.org
SO Journal of virology, (2003 Nov) 77 (21) 11625-32.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200312
ED Entered STN: 20031101
Last Updated on STN: 20031219
Entered Medline: 20031202

=> d 114 ab

L14 ANSWER 1 OF 1 MEDLINE on STN
AB To characterize epitopes on human papillomavirus (HPV) virus-like
particles (VLPs), a panel of mutated HPV-16 VLPs was
created. Each mutated VLP had residues substituted from HPV-31 or HPV-52
L1 sequences to the HPV-16 L1
backbone. Mutations were created on the HPV-31 and -52 L1
proteins to determine if HPV-16 type-specific
recognition could be transferred. Correct folding of the mutated proteins
was verified by resistance to trypsin digestion and by binding to one or
more conformation-dependent monoclonal antibodies. Several of the
antibodies tested were found to bind to regions already identified as
being important for HPV VLP recognition (loops DE, EF, FG, and HI).
Sequences at both ends of the long FG loop (amino acids 260 to 290) were
required for both H16.V5 and H16.E70 reactivity. A new antibody-binding
site was discovered on the C-terminal arm of L1 between
positions 427 and 445. Recognition of these residues by the H16.U4
antibody suggests that this region is surface exposed and supports a
recently proposed molecular model of HPV VLPs.

=> d 122 2 all

L22 ANSWER 2 OF 3 MEDLINE on STN
AN 97437475 MEDLINE
DN PubMed ID: 9292008
TI A monoclonal antibody against intact human papillomavirus type 16 capsids blocks the serological reactivity of most human sera.
AU Wang Z; Christensen N; Schiller J T; Dillner J
CS Microbiology and Tumorbiology Center, Karolinska Institute, Stockholm, Sweden.
SO Journal of general virology, (1997 Sep) 78 (Pt 9) 2209-15.
Journal code: 0077340. ISSN: 0022-1317.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199710
ED Entered STN: 19971013
Last Updated on STN: 19971013
Entered Medline: 19971001
AB A type-specific and neutralizing mouse MAb (V5) against human papillomavirus (HPV) type 16 capsids was found to block the serological reactivity of human sera with the corresponding capsids. Out of 352 human serum samples tested for the presence of IgG against HPV-16, more than 75% of reactive sera were completely blocked by the **V5 antibody**. Type-specific MAbs against HPV-6, -18 and -33 were also found to block serological reactivity with capsids of the corresponding HPV types for the majority of reactive human sera. The results suggest that most antibodies in human sera that are reactive with intact HPV capsids recognize the same or closely related major antigenic determinant(s).
CT Check Tags: Female; Human; Support, Non-U.S. Gov't
Adolescent
Adult
Animals
*Antibodies, Monoclonal
*Antibodies, Viral
Antibodies, Viral: BL, blood
Binding, Competitive
*Capsid: IM, immunology

d 123 1 5 all

L23 ANSWER 1 OF 7 MEDLINE on STN
AN 2004170965 MEDLINE
DN PubMed ID: 15063127
TI **HPV-16 L1** genes with inactivated negative
RNA elements induce potent immune responses.
AU Rollman Erik; Arnheim Lisen; Collier Brian; Oberg Daniel; Hall Hakan;
Klingstrom Jonas; Dillner Joakim; Pastrana Diana V; Buck Chris B; Hinkula
Jorma; Wahren Britta; Schwartz Stefan
CS Department of Virology, Swedish Institute for Infectious Disease Control,
Solna, Sweden.. erik.rollman@smi.ki.se
SO Virology, (2004 Apr 25) 322 (1) 182-9.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200406
ED Entered STN: 20040406
Last Updated on STN: 20040602
Entered Medline: 20040601
AB Introduction of point mutations in the 5' end of the human papillomavirus
type 16 (**HPV-16**) **L1** gene specifically
inactivates negative regulatory RNA processing elements. DNA vaccination
of C57Bl/6 mice with the **mutated L1** gene resulted in
improved immunogenicity for both neutralizing antibodies as well as for
broad cellular immune responses. Previous reports on the activation of
L1 by codon optimization may be explained by inactivation of the
regulatory RNA elements. The modified **HPV-16**
L1 DNA that induced anti-**HPV-16** immunity may
be seen as a complementary approach to protein subunit immunization
against papillomavirus.
CT Check Tags: Support, Non-U.S. Gov't
Animals
Antibodies, Viral: BL, blood
Antibodies, Viral: IM, immunology
CD4-Positive T-Lymphocytes: IM, immunology
CD8-Positive T-Lymphocytes: IM, immunology
Cells, Cultured
Disease Models, Animal
Genes, Regulator
Genes, Viral
Lymphocyte Activation
Mice
Mice, Inbred C57BL
Neutralization Tests
Oncogene Proteins, Viral: GE, genetics
*Oncogene Proteins, Viral: IM, immunology
Papillomavirus Infections: BL, blood
*Papillomavirus Infections: IM, immunology
Papillomavirus Infections: PC, prevention & control
Papillomavirus, Human: GE, genetics
*Papillomavirus, Human: IM, immunology
Point Mutation
Spleen: IM, immunology
*Vaccination
Vaccines, DNA: AD, administration & dosage
CN 0 (Antibodies, Viral); 0 (Oncogene Proteins, Viral); 0 (Vaccines, DNA); 0
(oncogene viral capsid protein, **L1** human papillomavirus type 16)

L23 ANSWER 5 OF 7 MEDLINE on STN

AN 2003149974 MEDLINE
DN PubMed ID: 12665934
TI Construction and identification of the replication-deficient recombinant
vaccinia virus co-expressing **HPV type 16**
L1 and **L2** proteins.
AU Han Liqun; Ren Jiao; Liang Yu; Tian Houwen; Zhi Huijun; Luo Weifeng; Lu
Zhenhua; Wei Lanlan; Ruan Li
CS Institute of Virology, Chinese Academy of Preventive Medicine, Beijing
100052, China.
SO Zhonghua shi yan he lin chuang bing du xue za zhi = Zhonghua shiyan he
linchuang bingduxue zazhi = Chinese journal of experimental and clinical
virology, (2002 Sep) 16 (3) 256-60.
Journal code: 9602873. ISSN: 1003-9279.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA Chinese
FS Priority Journals
EM 200311
ED Entered STN: 20030401
Last Updated on STN: 20031113
Entered Medline: 20031112
AB **OBJECTIVE:** To generate an HPV16 prophylactic vaccine candidate for
cervical cancer. **METHODS:** HPV16 major capsid protein **L1** gene
and minor capsid protein **L2** gene were amplified using PCR. These genes were
mutated by PCR site-directed mutagenesis for removal of sequence
motifs (TTTTTNT) which would cause transcription termination when
expressed from a vaccinia virus early promoter, then inserted into a
vaccinia virus expression vector. A strain replication-deficient
recombinant vaccinia virus containing the mutant sequences was obtained
through a homologous recombination and identified. **RESULTS:** The
nucleotide sequence remained the correct amino acid sequence of the
L1 and **L2** proteins after **mutated**. Full-length
L1 and **L2** proteins were generated in cells infected with the
recombinant virus. The virus strain propagated at very low titer or could
not reproduce in some kinds of cell derived from different human tissues.
CONCLUSIONS: The authors have generated a strain replication-deficient
recombinant vaccinia virus expressing HPV16 **L1** plus **L2** proteins
as an HPV16 prophylactic vaccine candidate for cervical cancer.
CT Check Tags: Female; Human; Support, Non-U.S. Gov't
Capsid
*Capsid Proteins: GE, genetics
Cell Line
Cervix Neoplasms: VI, virology
Cloning, Molecular
English Abstract
Gene Expression
Genetic Vectors

L25 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:581030 CAPLUS
DN 115:181030
TI Type-specific and cross-reactive epitopes in human papillomavirus type 16 capsid proteins
AU Beiss, Barbara K.; Heimer, Edgar; Felix, Arthur; Burk, Robert D.; Ritter, Diane B.; Mallon, Robert G.; Kadish, Anna S.
CS Dep. Pathol., Albert Einstein Coll. Med., Bronx, NY, 10461, USA
SO Virology (1991), 184(1), 460-4
CODEN: VIRLAX; ISSN: 0042-6822
DT Journal
LA English

=> d 125 2 ab

L25 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2004 ACS on STN
AB Rabbit polyclonal and mouse monoclonal antisera were raised to C terminal peptides from the genital human papillomavirus (HPV) 16 L1 and L2 open reading frames (ORFs). Anti-L1 and -L2 peptide sera recognized HPV 16 L1 and L2 fusion proteins in Western blots and by immunopptn. In Western blot anal. of L1 proteins from different HPV types, antisera to the L1 peptide reacted only with HPV 16, thus identifying an HPV 16 type-specific linear epitope. Anti-L2 peptide sera reacted with L2 fusion proteins from HPVs 6 and 16, but not from BPV, thus identifying a partially cross-reactive epitope in the HPV 16 L2. Computer anal. of C terminal amino acid sequences of the L1 and L2 ORFs of multiple HPV types supported the Western blot findings. Despite the HPV 16 type specificity found in Western blots, anti-L1 peptide sera identified nuclear antigen by immunocytochem. in cervical biopsies infected with HPV 16, as well as other genital HPV types. Anti-L2 peptide sera failed to recognize antigen in infected tissue.

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FILE 'MEDLINE' ENTERED AT 11:26:06 ON 12 AUG 2004

L1 2479 S PAPILLOMA VIRUS
L2 14951 S PAPILLOMAVIRUS
L3 3154 S HPV TYPE 16 OR HPV-16
L4 1758 S L1 AND L2
L5 0 S L3 AND DELETED EPITOPE
L6 0 S L3 AND DEVOID EPITOPE
L7 41 S L3 AND MODIFIED
L8 10 S L7 AND "L1"
L9 4 S ITSE
L10 0 S IMMUNODOMINANT TYPE SPECIFC EPITOPE
L11 0 S DEVOID SPECIFIC EPITOPE
L12 302 S L3 AND "L1"
L13 0 S SPECIFC EPITOPE AND L12
L14 1 S SPECIFIC EPITOPE AND L12
L15 0 S EPITOPE DEPELETED
L16 0 S EPITOPE DEPLETED
L17 0 S DEPLETED EPITOP?
L18 2 S DELETED EPITOP?
L19 0 S L18 AND L2
L20 0 S D9 ANTIBODY
L21 0 S "D9" ANTIBODY
L22 3 S "V5" ANTIBODY
L23 7 S L12 AND MUTATED

FILE 'BIOSIS' ENTERED AT 11:44:34 ON 12 AUG 2004

L24 1 S L14

FILE 'CAPLUS' ENTERED AT 11:44:59 ON 12 AUG 2004

L25 2 S L14

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File: DWPI

Mar 26, 2003

DERWENT-ACC-NO: 2001-281675

DERWENT-WEEK: 200327

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TITLE: Carrier for delivering substances to cells, useful in antitumor vaccines, comprises the major capsid protein of human papilloma virus modified to be nonimmunogenic

INVENTOR: ANTONSSON, P; DILLNER, J ; KRISTENSSON, K ; LANDO, P ; WALLEN-OHMAN, M ; WALLEN-OEHMAN, M

PRIORITY-DATA: 1999SE-0003534 (September 30, 1999)

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INT-CL (IPC): A61 K 39/00; A61 K 39/02; A61 K 39/12; A61 K 48/00; A61 P 1/00; A61 P 11/04; A61 P 15/00; A61 P 15/02; A61 P 31/04; A61 P 31/12; A61 P 33/00; A61 P 35/00; A61 P 35/04; C07 K 0/00; C07 K 14/025; C07 K 19/00; C12 N 15/09; C12 N 15/86

ABSTRACTED-PUB-NO: WO 200123422A

BASIC-ABSTRACT:

NOVELTY - Carrier (A) for introducing a substance (I) into cells comprising the major capsid protein (L1) of human papilloma virus (HPV) that has been engineered to remove major type-specific epitopes that cause production of neutralizing antibodies is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) vaccines containing (A) as active ingredient;
- (2) polynucleotides (II) that encode (A); and
- (3) vaccines containing (II) as active ingredient;
- (4) the prevention or treatment of viral bacterial or parasitic infections by vaccination with (A).
- (5) the prevention or treatment of cancer by vaccination with (A).

ACTIVITY - Antitumor; antiviral; antibacterial; antiparasitic.

MECHANISM OF ACTION - Cytotoxic. Induction of a specific cytotoxic T cell response.

USE - (A), or the nucleic acid that encodes them, are used in vaccines for prevention or treatment of

- (i) viral, bacterial or parasitic infections, specifically infection by HPV; or
- (ii) benign or malignant consequences of HPV infections (specifically warts; laryngeal papillomatosis, and cancer of cervix, penis, vulva, vagina, anus or oropharynx).

ADVANTAGE - (A) does not induce production of neutralizing antibodies against itself, and may induce a response that is cross-reactive to several different HPV serotypes.

ABSTRACTED-PUB-NO: WO 200123422A

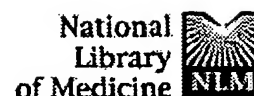
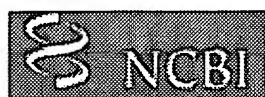
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 Primary screening for human papillomavirus infection.
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- ☐ 42: [Konya J, Dillner J.](#) Related Articles, Links
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 PMID: 11252250 [PubMed - indexed for MEDLINE]
- ☐ 47: [Harro CD, Pang YY, Roden RB, Hildesheim A, Wang Z, Reynolds MJ, Mast TC, Robinson R, Murphy BR, Karron RA, Dillner J, Schiller JT, Lowy DR.](#) Related Articles, Links
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